AMENDMENTS TO THE CLAIMS

Please amend the claims as indicated in the listing of pending claims presented below. This listing of claims replaces all prior versions and listings of claims in the above-referenced patent application. In accordance with 37 C.F.R. § 1.121, as revised on June 30, 2003, claims are labeled as "Original", "Currently amended", "Canceled", "Withdrawn", "Previously presented", "New", or "Not entered".

Listing of Claims

Claims 1 to 95 **(Canceled)**

96. **(Withdrawn)** A bifunctional molecule comprising at least one metal-chelating moiety associated with at least one amyloid-binding moiety, wherein the metal-chelating moiety binds with high affinity at least one transition metal ion selected from the group consisting of zinc II (Zn^{2+}), copper II (Cu^{2+}), and iron III (Fe^{3+}).

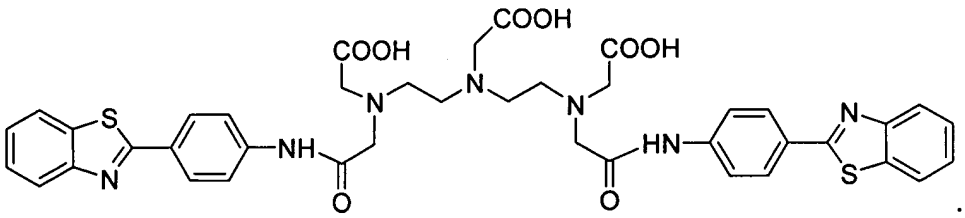
97. **(Withdrawn)** The bifunctional molecule of claim 96, wherein the metal-chelating moiety comprises DTPA.

98. **(Withdrawn)** The bifunctional molecule of claim 96, wherein the metal-chelating moiety comprises an α-lipoic acid derivative.

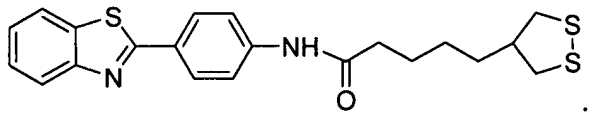
99. **(Withdrawn)** The bifunctional molecule of claim 96, wherein the amyloid-binding moiety is blood-brain barrier permeable.

100. **(Withdrawn)** The bifunctional molecule of claim 96, wherein the amyloid-binding moiety has a high affinity and specificity for Aβ amyloid deposits.

101. **(Withdrawn)** A bifunctional molecule with the following chemical structure:



102. **(Withdrawn)** A bifunctional molecule with the following chemical structure:



103. **(Withdrawn)** A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 1, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

104. **(Withdrawn)** A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 101, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

105. **(Withdrawn)** A pharmaceutical composition comprising an effective amount of at least one bifunctional molecule of claim 102, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

106. **(Withdrawn)** A method for reducing or inhibiting amyloid toxicity in a system, comprising contacting the system with a bifunctional molecule of claim 1, or a pharmaceutical composition thereof.

107. **(Withdrawn)** The method of claim 106, wherein said method prevents, slows down or stops amyloid accumulation in the system, or promotes, induces, or otherwise facilitates dissolution of amyloid deposits present in the system; or both.

108. **(Withdrawn)** The method of claim 106, wherein said method reduces, inhibits or otherwise interferes with amyloid-mediates production of reactive oxygen species.

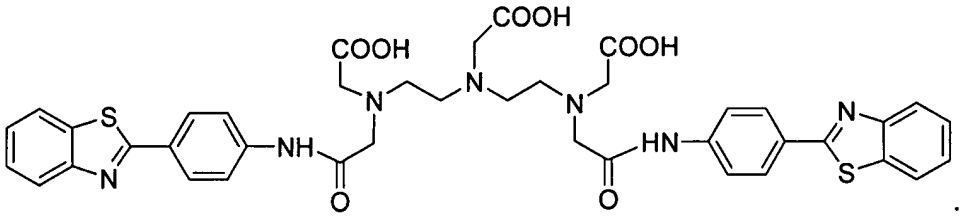
109. **(Withdrawn)** The method of claim 106, wherein the contacting is carried out by *in vitro* or ex vivo incubation, and wherein the system is selected from the group consisting of a cell, a biological fluid, and a biological tissue.

110. **(Withdrawn)** The method of claim 109, wherein the cell, biological fluid, or biological tissue originates from a patient suspected of having a pathophysiological condition associated with amyloid accumulation.

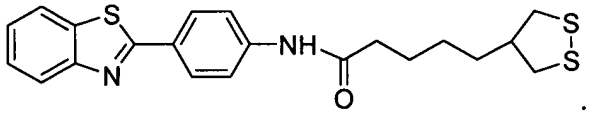
111. **(Withdrawn)** The method of claim 110, wherein the pathophysiological condition is

associated with accumulation of amyloid-b peptide, and wherein the amyloid-binding moiety in the bifunctional molecule has a high affinity and specificity for Aβ amyloid deposits.

112. **(Withdrawn)** The method of claim 106, wherein the bifunctional molecule has the following chemical structure:



113. **(Withdrawn)** The method of claim 106, wherein the bifunctional molecule has the following chemical structure:



114. **(Withdrawn)** A method for treating a patient with a pathophysiological condition associated with amyloid accumulation, comprising administering to the patient an effective amount of a bifunctional molecule of claim 1, or a pharmaceutical composition thereof.

115. **(Withdrawn)** The method of claim 114, wherein said method prevents, slows down, or stops amyloid accumulation in the patient; or promotes, induces, or otherwise facilitates dissolution of amyloid deposits present in the patient; or both.

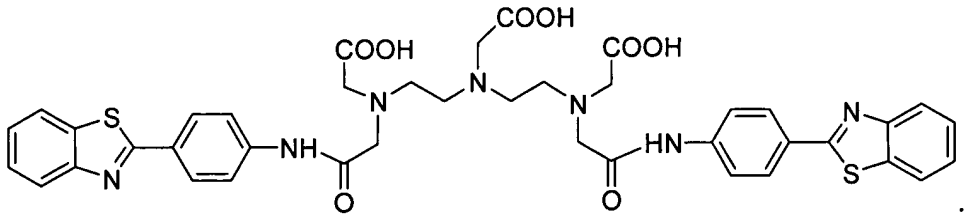
116. **(Withdrawn)** The method of claim 114, wherein said method reduces, inhibits or otherwise interferes with amyloid-mediated production of reactive oxygen species.

117. **(Withdrawn)** The method of claim 114, wherein the administration is carried out by a method selected from the group consisting of oral administration and parenteral administration.

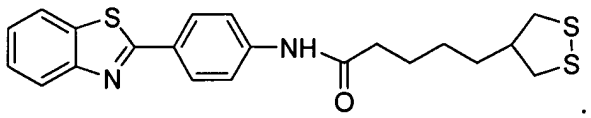
118. **(Withdrawn)** The method of claim 114, wherein the pathophysiological condition is associated with accumulation of amyloid-β peptide, and wherein the amyloid-binding

moiety in the bifunctional molecule has a high affinity and specificity for Aβ amyloid deposits.

119. **(Withdrawn)** The method of claim 114, wherein the bifunctional molecule has the following chemical structure:



120. **(Withdrawn)** The method of claim 114, wherein the bifunctional molecule has the following chemical structure:



121. **(Withdrawn)** The method of claim 114, wherein the pathophysiological condition is selected from the group consisting of Alzheimer's disease, Down's syndrome, Lewy body dementia, hereditary cerebral hemorrhage with amyloidosis (Dutch type), Guam Parkinson-Dementia, and head trauma.

122. **(Withdrawn)** The method of claim 114, wherein the pathophysiological condition is Alzheimer's disease.

123. **(Currently Amended)** A contrast imaging agent comprising at least one imaging moiety covalently associated with at least two ~~at least one~~ amyloid-binding moieties. ~~moiety.~~

124. **(Currently Amended)** The contrast imaging agent of claim 123, wherein the amyloid-binding moieties are ~~moiety is~~ blood-brain barrier permeable.

125. **(Currently Amended)** The contrast imaging agent of claim 123, wherein the amyloid-binding moieties have ~~moiety has~~ a high affinity and specificity for Aβ amyloid deposits.

126. **(Previously Presented)** The contrast imaging agent of claim 123, wherein the imaging moiety comprises at least one metal-chelating moiety complexed to a metal entity.

127. **(Previously Presented)** The contrast imaging agent of claim 126, wherein the metal-chelating moiety comprises DTPA.

128. **(Currently Amended)** The contrast imaging agent of claim 123, wherein the imaging moiety comprises at least one metal-chelating moiety complexed to a metal entity, and wherein the amyloid-binding moieties have ~~moiety has~~ a high affinity and specificity for Aβ amyloid deposits.

129. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is a paramagnetic metal ion.

130. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is a paramagnetic metal ion selected from the group consisting of gadolinium III (Gd^{3+}), chromium III (Cr^{3+}), dysprosium III (Dy^{3+}), iron III (Fe^{3+}), manganese II (Mn^{2+}), and ytterbium III (Yb^{3+}).

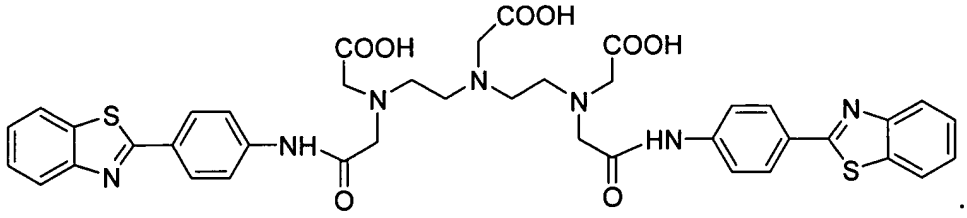
131. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is gadolinium III (Gd^{3+}).

132. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is a radionuclide.

133. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is a radionuclide selected from the group consisting of technetium-99m (^{99m}Tc), gallium-67 (^{67}Ga), yttrium-91 (^{90}Y), indium-111 (^{111}In), rhenium-186 (^{186}Re), and thallium-201 (^{201}Tl).

134. **(Previously Presented)** The contrast imaging agent of claim 126 or 128, wherein the metal entity is technetium-99 (^{99m}Tc).

135. **(Currently Amended)** A contrast imaging agent, wherein a metal entity ~~gadolinium III (Gd^{3+})~~ is complexed to a bifunctional molecule with the following chemical structure:



136. **(Currently Amended)** A contrast imaging agent comprising at least one metal-chelating moiety covalently associated with at least two ~~at least one~~ amyloid-binding moieties ~~moiety~~ labeled with a stable paramagnetic isotope.

137. **(Previously Presented)** The contrast imaging agent of claim 136, wherein the stable paramagnetic isotope is carbon-13 (^{13}C) or fluorine-19 (^{19}F).

138. **(Previously Presented)** A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 123, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

139. **(Previously Presented)** A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 126, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

140. **(Previously Presented)** A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 130, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

141. **(Previously Presented)** A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 133, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

142. **(Previously Presented)** A pharmaceutical composition comprising an imaging effective amount of at least one contrast imaging agent of claim 135, or a physiologically tolerable salt thereof, and at least one pharmaceutically acceptable carrier.

143. **(Withdrawn)** A method for detecting the presence of amyloid deposits in a system comprising steps of:

contacting the system with an imaging effective amount of a contrast imaging agent of claim 126, or a pharmaceutical composition thereof, under conditions to allow the contrast imaging agent to interact with any amyloid deposit present so that the interaction results in binding of the contrast imaging agent to the amyloid deposit;

detecting any amyloid deposit present in the system and bound to the contrast

imaging agent, using an imaging technique; and

generating one or more images of at least part of the system.

144. **(Withdrawn)** The method of claim 143, wherein the amyloid deposits present in the system are formed by accumulation of amyloid-β peptide, and wherein the amyloid-binding moiety in the contrast imaging agent has a high affinity for Aβ amyloid deposits.

145. **(Withdrawn)** The method of claim 143, wherein the contacting is carrier out by in vivo or ex vivo incubation, and wherein the system is selected from the group consisting of a cell, a biological fluid, and biological tissue.

146. **(Withdrawn)** The method of claim 145, wherein the cell, biological fluid, or biological tissue originates from a patient suspected of having a pathophysiological condition associated with amyloid accumulation.

147. **(Withdrawn)** The method of claim 145, wherein the cell, biological fluid, or biological tissue originates from a patient receiving a treatment for a pathophysiological condition associated with amyloid accumulation.

148. **(Withdrawn)** The method of claim 145, wherein the cell, biological fluid, or biological tissue has been contacted with a potential therapeutic agent for the treatment of a pathophysiological condition associated with amyloid accumulation.

149. **(Withdrawn)** The method of claim 143, wherein said method is used to identify potential therapeutic agents for the treatment of a pathophysiological condition associated with amyloid accumulation.

150. **(Withdrawn)** The method of claim 143, wherein said method is used to diagnose a pathophysiological condition associated with amyloid accumulation.

151. **(Withdrawn)** The method of claim 143, wherein said method is used to follow the progression of a pathophysiological condition associated with amyloid accumulation.

152. **(Withdrawn)** The method of claim 143, wherein said method is used to monitor the response of a patient to a treatment for a pathophysiological condition associated with amyloid accumulation.

153. **(Withdrawn)** A method for detecting the presence of amyloid deposits in a patient comprising steps of:

administering to the patient an imaging effective amount of a contrast imaging agent of claim 126, or a pharmaceutical composition thereof, under conditions to allow the contrast imaging agent to interact with any amyloid deposit present so that the interaction results in binding of the contrast imaging agent to the amyloid deposit;

detecting any amyloid deposit present in the patient and bound to the contrast imaging agent, using an imaging technique; and

generating one or more images of at least part of the body of the patient.

154. **(Withdrawn)** The method of claim 153, wherein the administration is carried out by a method selected from the group consisting of oral administration and parenteral administration.

155. **(Withdrawn)** The method of claim 153, wherein the amyloid deposits are formed by aggregation and accumulation of amyloid-β peptide, and wherein the amyloid-binding moiety in the contrast imaging agent has a high affinity or specificity for Aβ amyloid deposits.

156. **(Withdrawn)** The method of claim 153, wherein said method is used to localize amyloid deposits in a patient.

157. **(Withdrawn)** The method of claim 153, wherein said method is used to localize amyloid deposits in the brain of a patient, and wherein the amyloid-binding moiety in the contrast imaging agent is blood-barrier permeable.

158. **(Withdrawn)** The method of claim 153, wherein said method is used to diagnose a pathophysiological condition associated with amyloid accumulation.

159. **(Withdrawn)** The method of claim 153, wherein said method is used to follow the progression of a pathophysiological condition associated with amyloid accumulation.

160. **(Withdrawn)** The method of claim 153, wherein said method is used to monitor the response of a patient to a treatment for a pathophysiological condition associated with

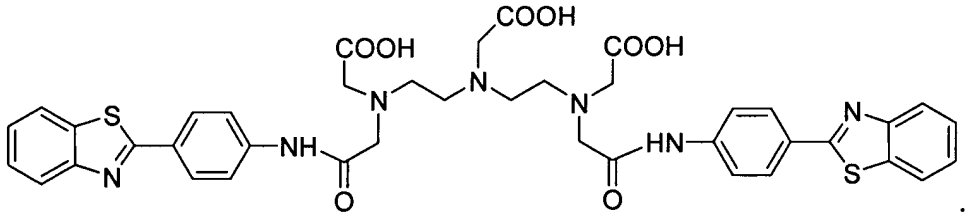
amyloid accumulation.

161. **(Withdrawn)** The method of claim 143 or 153, wherein the imaging moiety in the contrast imaging agent comprises at least one metal-chelating moiety complexed to a paramagnetic metal ion; detecting comprises using Magnetic Resonance Imaging (MRI); and MR images are generated.

162. **(Withdrawn)** The method of claim 161, wherein the paramagnetic metal ion is selected from the group consisting of gadolinium III (Gd^{3+}), chromium III (Cr^{3+}), dysprosium III (Dy^{3+}), iron III (Fe^{3+}), manganese II (Mn^{2+}), and ytterbium III (Yb^{3+}).

163. **(Withdrawn)** The method of claim 161, wherein the paramagnetic metal ion is gadolinium III (Gd^{3+}).

164. **(Withdrawn)** The method of claim 163, wherein gadolinium III (Gd^{3+}) is complexed to a bifunctional molecule with the following chemical structure:



165. **(Withdrawn)** The method of claim 143 or 153, wherein the imaging moiety in the contrast imaging agent comprises at least one metal-chelating moiety complexed to a radionuclide; detecting comprises using Single Photon Emission Computed Tomography (SPECT); and SPECT images are generated.

166. **(Withdrawn)** The method of claim 165, wherein the radionuclide is selected from the group consisting of technetium-99m (^{99m}Tc), gallium-67 (^{67}Ga), yttrium-91 (^{90}Y), indium-111 (^{111}In), rhenium-186 (^{186}Re), and thallium-201 (^{201}Tl).

167. **(Withdrawn)** The method of claim 165, wherein the radionuclide is technetium-99m (^{99m}Tc).

168. **(Withdrawn)** The method of claim 149, 150, 151, 152, 158, 159 or 160, wherein the pathophysiological condition is associated with accumulation of amyloid-β peptide, and

wherein the amyloid-binding moiety in the contrast imaging agent has a high affinity for Aβ amyloid deposits.

169. **(Withdrawn)** The method of claim 149, 150, 151, 152, 158, 159 or 160, wherein the pathophysiological condition is selected from the group consisting of Alzheimer's disease, Down's syndrome, Lewy body dementia, hereditary cerebral hemorrhage with amyloidosis (Dutch type), Guam Parkinson-Dementia, and head trauma.

170. **(Withdrawn)** The method of claim 149, 150, 151, 158, 159 or 160, wherein the pathophysiological condition is Alzheimer's disease.

171. (**New**) The contrast imaging agent of claim 135, wherein the metal entity is a paramagnetic metal ion selected from the group consisting of gadolinium III (Gd^{3+}), chromium III (Cr^{3+}), dysprosium III (Dy^{3+}), iron III (Fe^{3+}), manganese II (Mn^{2+}), and ytterbium III (Yb^{3+}).

172. (**New**) The contrast imaging agent of claim 135, wherein the metal entity is gadolinium III (Gd^{3+}).

173. (**New**) The contrast imaging agent of claim 135, wherein the metal entity is a radionuclide selected from the group consisting of technetium-99m (^{99m}Tc), gallium-67 (^{67}Ga), yttrium-91 (^{90}Y), indium-111 (^{111}In), rhenium-186 (^{186}Re), and thallium-201 (^{201}Tl).

174. (**New**) The contrast imaging agent of claim 135, wherein the metal entity is technetium-99 (^{99m}Tc).